

PATENT COOPERATION TREATY
PCT
INTERNATIONAL SEARCH REPORT
(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 29399-0077	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below
International application No. PCT/CA2004/002196	International filing date (<i>day/month/year</i>) 23 December 2004 (23-12-2004)	(Earliest) Priority date (<i>day/month/year</i>) 23 December 2003 (23-12-2003)
Applicant MEDICURE INTERNATIONAL INC. ET AL		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 7 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☒ Certain claims were found unsearchable (see Box No. II).

3. ☒ Unity of invention is lacking (see Box No. III).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows :

COMBINATION THERAPIES EMPLOYING A COMPOSITION COMPRISING A HMG COA REDUCTASE INHIBITOR
AND A VITAMIN B6 RELATED COMPOUND

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,

- a. the figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ as selected by this authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2004/002196

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of the first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons :

1. ☒ Claim Nos. : 8-37

because they relate to subject matter not required to be searched by this Authority, namely :

Although claims 8-37 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition as described in Examples 2-4 of the description.

2. ☒ Claim Nos. : 1-37 (part)

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically :

see PCT/ISA/210 (Extra Sheet)

3. ☐ Claim Nos. :

because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows :

see PCT/ISA/210 (Extra Sheet)

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claim Nos. :
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim Nos. :

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2004/002196

A. CLASSIFICATION OF SUBJECT MATTER

IPC⁷ A61K 31/675, A61K 31/366, A61K 31/4412, A61K 31/4415, A61K 31/4355, A61P 9/00

According to International Patent Classification (IPC) or to both national classification and IPC⁷

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC⁷ A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
Delphion, Science Citation Index Expanded, PubMed, Canadian Patent Database; *keywords*: statin, HMG-CoA, cholesterol, cardiovascular, vitamin, vitamin B6, PLP, pyridoxal-5'-phosphate, pyridoxine, pyridoxal, pyridoxamine

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No(s).
P, X	WO 04/006919 (KONDO et al) 22 January 2004 (2004-01-22) *see entire application*	1-4, 8-17, 19-20, 24-27, 31-37 (part)
Y	Canadian Journal of Cardiology, 1995, Vol. 11 (Supp C), FROHLICH, "Lipoproteins and homocyst(e)ine as risk factors for atherosclerosis: Assessment and treatment", pages 18C-23C *see entire article*	1-18 (part)
Y	WO 00/57863 (DHALLA) 5 October 2000 (2000-10-05) *see entire application*	1-4, 8-15, 19-20, 24-27, 31-37 (part)
Y	WO 00/53606 (HAQUE) 14 September 2000 (2000-09-14) *see entire application*	1-3, 5-6, 8-15, 19, 21-22, 24-26, 28-29, 31-37 (part)

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent but published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

30 March 2005 (30-03-2005)

Date of mailing of the international search report

10 May 2005 (10-05-2005)

Name and mailing address of the ISA/CA
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA2004/002196

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No(s).
Y	WO 01/64692 (HAQUE) 7 September 2001 (2001-09-07) *see entire application*	1-3, 7-16, 19, 23-26, 30-37 (part)
Y	Lipids in Health and Disease, 18 September 2003, Vol 2(7), DUMM et al., "Variations in the lipid profile of patients with chronic renal failure treated with pyridoxine", pages 1-6 *see page 2 of 6*	1-37 (part)
Y	US 5288716 (SPECK), 22 February 1994 (1994-02-22) *see entire application*	1-37 (part)
Y	Journal of Lipid Research, 1 September 2003, (2003-09-01), Vol. 44, CHAUHAN, "Membrane dynamics, cholesterol homeostasis, and Alzheimer's disease", pages 2019-2029 *see pages 2024-2025*	17 (part)
Y	Injury Prevention, 2002, Vol. 8, pages 276-279, RAY et al., "Lipid- lowering agents and the risk of hip fracture in a Medicaid population", pages 276-279 *see abstract, page 279*	18 (part)
A	WO 97/38694 (TOBERT) 23 October 1997 (1997-11-23) *see entire application*	1-18 (part)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2004/002196

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
WO04006919	01-22-2004	JP2004189716 A2	07-08-2004
		CA2492781 AA	01-22-2004
		AU3281176 AA	02-02-2004
WO0057863	5-10-2000	AT259643T T	15-03-2004
		AU759824 B2	01-05-2003
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		AU3314700 A	16-10-2000
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		BR0009292 A	26-12-2001
		CA2254528 A1	09-01-2000
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		CN1208922 A	24-02-1999
		DE60008352D D1	25-03-2004
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		DK1162980T T3	14-06-2004
		EP1162980 A2	19-12-2001
		ES2215618T T3	16-10-2004
		JP11029828 A	02-02-1999
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		NZ514767 A	27-02-2004
		PT1162980T T	30-06-2004
		SG89259 A1	18-06-2002
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		US6043259 A	28-03-2000
		US6066229 A	23-05-2000
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WO0053606	14-09-2000	AU763464 B2	24-07-2003
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		US2001031770 A1	18-10-2001
		US2003195236 A1	16-10-2003
WO0164692	07-09-2001	AU3718501 A	12-09-2001
		CA2401655 A1	07-09-2001
		EP1268498 A1	02-01-2003
		JP2003525303T T	26-08-2003
		US6605612 B2	12-08-2003
		US6667315 B2	23-12-2003
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INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2004/002196

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
US5288716	22-02-1994	AT82125T T	15-11-1992
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		DE3705549 A1	01-09-1988
		DE3875760D D1	17-12-1992
		DK55888 A	19-08-1988
		EG18335 A	30-09-1992
		EP0282696 A2	21-09-1988
		ES2052609T T3	16-07-1994
		GR3006693T T3	30-06-1993
		HU47850 A2	28-04-1989
		JP2005061C C	11-01-1996
		JP2588686B2 B2	05-03-1997
		KR9509094 B1	14-08-1995
		US6066659 A	23-05-2000
		ZA8800577 A	28-07-1988
WO9738694	23-10-1997	AU732465 B2	26-04-2001
		AU2666597 A	07-11-1997
		CA2251972 A1	23-10-1997
		EP0904082 A1	31-03-1999
		GB9612082D D0	14-08-1996
		GB9616804D D0	25-09-1996
		JP2000508659T T	11-07-2000
		US6673831 B1	06-01-2004

Continuation of Box No. II Part 2.

Claims 1, 2-23 (part), 24, 25-37 (part):

Claims 1, 24 do not meet the requirements of Article 6 PCT because the subject-matter is defined in terms of the result to be achieved rather than in terms of technical features, as required by Rule 6.3(a) PCT. Thus, the following expressions are considered to be functional features:

“HMG CoA reductase inhibitor”; and “vitamin B6 related compound”.

Since the components of the pharmaceutical composition of claim 1 and use thereof in the method of claim 24 are defined solely by reference to desirable characteristics, namely as “HMG CoA reductase inhibitor” and “vitamin B6 related compound” a meaningful search over the whole of the claimed scope within the meaning of Article 6 PCT for claims 1, 24 is impossible. Furthermore, the use of the expression “analogue” (claim 3) in the present context is also considered to lead to a lack of clarity within the meaning of Article 6. The lack of clarity with respect to the functional claiming and ambiguous definitions is such as to render a meaningful and complete search impossible. Due to the multiple meanings that can be arrived at for “HMG CoA reductase inhibitor”; “vitamin B6 related compound”; “3-acylated analogue of pyridoxal”; “3-acylated analogue of pyridoxal-4,5-aminal”, and “pyridoxine phosphate analogue”, a complete prior art search was precluded and limited to those components of the composition that appear to be supported. Therefore, the search was limited to those pharmaceutical compositions and method of use therein comprising the HMG CoA reductase inhibitors defined in claim 2, and the vitamin B6 related compounds: pyridoxal, pyridoxal-5'-phosphate, or pyridoxamine of claim 3, the 3-acylated analogues of pyridoxal defined in claim 5, the 3-acylated analogues of pyridoxal-4,5-aminal defined in claim 6, and the pyridoxine phosphate analogues defined in claim 7, for the pharmaceutical compositions and method of use therein defined in claims 1-37.

Continuation of Box No. III

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Group A: Claims 1-18 are directed to a pharmaceutical composition comprising a HMG CoA reductase inhibitor and a vitamin B6 related compound and methods of use therein.

Group B: Claims 19-37 are directed to a method of treating or preventing hypercholesterolemia and a method of treating a patient at risk of cardiovascular disease, said patient at risk of cardiovascular disease already taking a HMG CoA reductase inhibitor, comprising administering a therapeutically effective dose of a vitamin B6 related compound.